

Application No. 09/498,046  
Response Dated January 23, 2006 to  
July 21, 2005 Office Action

**Amendments to the Claims**

Please amend claims 26-32, 34, 36-41, 46, and 52-57 and add claim 58 as follows.

This listing of claims will replace all prior versions, and listings, of claims in this application.

**Listing of Claims:**

1-25. (Cancelled)

26. (Currently Amended) A method for reducing the severity or lethal potential of a A-human influenza vaccine infection comprising the step of administering to a person at risk of such infection, in an amount effective for said reduction, a composition comprising a fusion product, said fusion product comprising

(i) an immunogenic extracellular part of (a) an M2 membrane protein of a human influenza A virus, (b) an NB protein of a human influenza B virus, or (c) a CM2 protein of a human influenza C virus, and

(ii) a heterologous presenting carrier.

27. (Currently Amended) The influenza vaccine of method according to claim 26, wherein the presenting carrier is a peptide or polypeptide.

28. (Currently Amended) The influenza vaccine of method according to claim 27, wherein the presenting peptide or polypeptide is selected from the group consisting of a hepatitis B core protein, C3d, polypeptides comprising multiple copies of C3d, tetanus toxin fragment C and yeast Ty particles.

29. (Currently Amended) The influenza vaccine of method according to claim 26, wherein the presenting carrier is a non-peptidic structure.

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30. (Currently Amended) The ~~influenza vaccine of~~ method according to claim 29, wherein the presenting non-peptidic structure is selected from the group consisting of glycans, polyethylene glycols, peptide mimetics, and synthetic polymers.

31. (Currently Amended) The ~~influenza vaccine of~~ method according to claim 26, wherein the presenting carrier enhances the immunogenicity of the antigen.

32. (Currently Amended) The ~~influenza vaccine of~~ method according to claim 31, wherein the presenting carrier comprises an epitope recognized by an influenza-specific T helper cell or cytotoxic T cell.

33. (Cancelled)

34. (Currently Amended) The ~~influenza vaccine of~~ method according to claim 26, wherein the ~~vaccine composition~~ comprises Lactococci cells expressing said fusion product in or on their cell membrane, and said cells optionally release said fusion product.

35. (Cancelled)

36. (Currently Amended) The ~~influenza vaccine of~~ method according to claim 26, wherein the fusion product is in an isolated form.

37. (Currently Amended) The ~~influenza vaccine of~~ method according to claim 26, wherein the fusion product is anchored in the membrane of an acceptor cell expressing the fusion product.

38. (Currently Amended) The ~~influenza vaccine of~~ method according to claim 26, wherein the fusion product is part of a lipid bilayer or cell wall.

39. (Currently Amended) The ~~influenza vaccine of method according to claim 26, wherein the influenza vaccine~~ composition comprises Lactococci cells expressing the fusion product in or on their cell wall.

40. (Currently Amended) The ~~influenza vaccine of method according to claim 26, further comprising an influenza antigen selected from the group consisting of hemagglutinin, neuraminidase, nucleoprotein and native M2.~~

41. (Currently Amended) A method of ~~obtaining a human influenza vaccine for preparing a composition for reducing the severity or lethal potential of a human influenza infection in a person at risk for such infection, comprising the steps of:~~

providing a fusion product, said fusion product comprising (i) an immunogenic extracellular part of (a) an M2 membrane protein of a human influenza A virus, (b) an NB protein of a human influenza B virus, or (c) a CM2 protein of a human influenza C virus, and (ii) a heterologous presenting carrier; and

mixing it with an excipient.

42. (Withdrawn) A nucleic acid construct encoding a fusion product, said fusion product comprising

(i) an extracellular part of an influenza M2 membrane protein or a functional fragment thereof or modified versions thereof, and

(ii) a presenting carrier,

wherein said extracellular part contains all or part of the 23 amino acid extracellular domain (amino acid residues 2 to 24 as shown in Table 1) of an M2 protein of influenza A virus or of a similar integral membrane protein of influenza B or C virus, and

wherein said functional fragment is a fragment of an M2 protein capable of eliciting a statistically significant higher immunoprotection when administered in an

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immunoprotective dose to test members of a species, as compared to test members of said species not receiving the functional fragment, and

wherein said modified versions comprise one to three amino acid changes but still react with a polyclonal antiserum derived from immunized animals.

43. (Withdrawn) The nucleic acid construct of claim 42, wherein the presenting carrier is a (poly)peptide.

44. (Withdrawn) A method of obtaining an influenza antigen, comprising:  
providing the nucleic acid construct of claim 42;  
introducing the nucleic acid construct into an acceptor cell;  
culturing the acceptor cell under conditions that allow expression of the fusion product; and

optionally isolating the fusion product from the acceptor cell or its culture medium, thereby obtaining an influenza antigen comprising the fusion product.

45. (Withdrawn) The method of claim 44, wherein the acceptor cell is a Lactococcus cell.

46. (Currently Amended) A human influenza vaccine obtained method for reducing the severity or lethal potential of a human influenza infection comprising the step of administering to a person at risk of such infection, in an amount effective for said reduction, a composition produced by the following steps:

providing a nucleic acid construct that encodes a fusion product, said fusion product comprising (i) an immunogenic extracellular part of (a) an M2 membrane protein of a human influenza A virus, (b) an NB protein of a human influenza B virus, or (c) a CM2 protein of a human influenza C virus, and (ii) a heterologous presenting peptide;

introducing the nucleic acid construct into an acceptor cell;

culturing the acceptor cell under conditions that allow expression of the fusion product;  
optionally isolating the fusion product from the acceptor cell or its culture medium;  
and  
optionally admixing the fusion product with an excipient,  
thereby obtaining a human influenza vaccine composition comprising the fusion product.

47. (Withdrawn) An acceptor cell containing the nucleic acid construct of claim 42.

48. (Withdrawn) The acceptor cell of claim 47, wherein the acceptor cell is a Lactococcus cell.

49. (Withdrawn) A method of obtaining a DNA-based or vaccinia-based influenza vaccine, comprising:

providing the nucleic acid construct of claim 42;  
introducing the nucleic acid construct into a host cell; and  
culturing the host cell under conditions that allow replication of the nucleic acid construct, thereby obtaining a DNA-based or vaccinia-based influenza vaccine comprising the nucleic acid construct.

50. (Withdrawn) A DNA-based influenza vaccine comprising the nucleic acid construct of claim 42.

51. (Withdrawn) A vaccinia-based influenza vaccine comprising the nucleic acid construct of claim 42.

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52. (Currently Amended) The ~~influenza vaccine of~~ method according to claim 26, wherein the ~~influenza vaccine composition~~ composition additionally comprises a cytokine.

53. (Currently Amended) The ~~influenza vaccine of~~ method according to claim 26, wherein the ~~influenza vaccine composition~~ composition additionally comprises a vaccine adjuvant that is not Freund's adjuvant.

54. (Currently Amended) ~~An influenza vaccine for an animal species~~ A method for reducing the severity or lethal potential of a non-human animal influenza infection comprising the step of administering to a non-human animal at risk of such infection, in an amount effective for said reduction, a composition comprising a fusion product, said fusion product comprising

- (i) an immunogenic extracellular part of (a) an M2 membrane protein of an influenza A virus or (b) an NB protein of an influenza B virus of said animal species; and
- (ii) a heterologous presenting carrier.

55. (Currently Amended) The ~~influenza vaccine of~~ method according to claim 26, wherein the fusion product comprises the entire extracellular domain of the M2 protein.

56. (Currently Amended) The ~~influenza vaccine of~~ method according to claim 55, wherein the amino acid sequence of said entire extracellular domain is SEQ ID NO:1, 2, or 3.

57. (Currently Amended) The ~~influenza vaccine of~~ method according to claim 26, wherein the fusion product comprises the entire extracellular domain of the NB or CM2 protein.

58. (New) The method according to any of claims 26 to 32 wherein the human influenza infection is type A and the fusion product comprises an immunogenic extracellular part of an M2 membrane protein of a human influenza A virus.